Fall Risk, Vestibular Schwannoma, and Anticoagulation Therapy

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Abstract

Elderly patients with balance problems are at high risk for falls. When these same patients are also on anticoagulants, the consequences of a fall can be serious. Anticoagulant therapy increases the risk of cerebral hemorrhage. Even mild head trauma can cause a fatal cerebral hemorrhage when anticoagulants are used. However, this risk needs to be weighed against the possibility of spontaneous stroke. The decision to choose anticoagulant therapy can become even more complicated if the patient has an increased risk of falling. A case is presented of an 87-year-old female with balance problems, in part from a small unilateral vestibular schwannoma. She was also receiving Coumadin anticoagulant therapy. When she began to fall, a decision had to be made about the relative risks and benefits of Coumadin therapy. The risk/benefit calculation could change, however, depending on whether her fall risk could be improved. This article presents the diagnostic test results and medical opinions surrounding this case. The importance of assessing patients’ overall situation is stressed in planning rehabilitation.

Key Words: Atrial fibrillation, Coumadin (brand name of generic warfarin), intracanalicular mass, fall risk, vestibular evoked myogenic potential, vestibular schwannoma

Abbreviations: CDP = computerized dynamic posturography; VEMP = vestibular evoked myogenic potential

Sumario

Los pacientes ancianos con problemas del equilibrio tienen un alto riesgo para caídas. Cuando esos mismos pacientes toman anticoagulantes, las consecuencias de una caída pueden ser serias. La terapia anticoagulante aumenta el riesgo de una hemorragia cerebral. Aún un trauma cefálico leve puede causar una hemorragia cerebral fatal cuando se usan anticoagulan-
Fall risk increases with age. In an otherwise healthy population, the risk of annual falls is an estimated 30 percent for those aged 65–75 years (Stevens et al, 2006) and up to 42 percent for those over age 75 (Blake et al, 1988; Shepard and Telian, 1996). For individuals over age 65, fall injuries are the fifth leading cause of death (Aschkenasy and Rothenhaus, 2006). Several factors increase fall risk in the elderly (Tinetti et al, 1988). Among them are instability and dizziness (O’Loughlin et al, 1993; Larsen et al, 2004; Pluijm et al, 2006). Similarly, cognitive changes including depression, stress, and dementia, whether physiologic or medication induced, also increase fall risk (Stalenhoef et al, 2002; French et al, 2006; Rubenstein and Josephson, 2006; Oliver et al, 2007; Sambrook et al, 2007).

Stroke risk also increases with age. Some forms of co-occurring heart disease, most commonly atrial fibrillation, increase stroke risk by increasing the likelihood of clot formation (cardiogenic emboli). To reduce the risk of cardiogenic emboli formation in at-risk patients, anticoagulation medications such as Coumadin (warfarin) are widely prescribed (Karni et al, 2001; Lew and Lim, 2002). Unfortunately, anticoagulation therapy may also increase the risk for intracranial hemorrhaging following traumatic head injury (Gage et al, 2005; Parmar et al, 2006). In one study, anticoagulation therapy prior to head injury was shown to increase patients’ risk of death to four to five times higher than that of non-anticoagulated patients (Parmar et al, 2006). Among patients age 80 and older, falling was the most often physician-cited reason for not prescribing anticoagulants (Garvin and Howard, 2006). However, epidemiological studies indicate that despite the increased risk for traumatic intracranial hemorrhage, anticoagulation therapy benefits in terms of preventing spontaneous neurovascular and cardiovascular catastrophes usually outweigh the risks (Gage et al, 2005). Nevertheless, the risks and benefits must be weighed in each individual case.

Vestibular schwannoma (also often referred to as acoustic neuroma) is a benign tumor of the eighth cranial nerve, specifically arising from the vestibular division. Its incidence in the general population is approximately 1 in 100,000 per year (Nestor et al, 1988; Howitz et al, 2000; Tos et al, 2004). Vestibular schwannomas are typically slow growing (~1 mm per year) and can present with slowly progressive hearing loss, imbalance, and dizziness but rarely vertigo (Nedzelski et al, 1992). The vestibular symptoms are due to the fact that the tumor arises from the vestibular portion of the eighth cranial nerve, thereby disrupting the labyrinthine signal to the brain stem nuclei, resulting in an asymmetrical labyrinthine
input into the central nervous system.

This case report presents a patient who was on Coumadin therapy, was experiencing imbalance and falls, and was found to have a left intracanalicular vestibular schwannoma. She was at obvious risk for head trauma. Without Coumadin anticoagulation, she was also at risk for clot formation and potentially a stroke or other emboli-related complications (pulmonary embolus, peripheral vascular embolus, etc.). Because of the need to make a management decision concerning continued Coumadin therapy, an effort was made to identify risk factors for falling that could be modified. The audiologic, vestibular, and otologic evaluations contributed to this aim but were not definitive. Rather, the viewpoints of several disciplines were required to come to a decision concerning the relative value and risks of anticoagulation therapy in this patient with heightened fall risk.

**CASE REPORT**

An 87-year-old independently living female presented to the Mayo Clinic Florida with concerns of disorientation and memory difficulties. Additionally, she complained of long-standing postural instability and a two-year history of falling. Two years prior she had fallen and broken her right kneecap. She was essentially bedridden for several months. She felt that she had become increasingly unsteady and had fallen more since this injury. Finally, she had a history of cardiac arrhythmia and a seven-year history of Coumadin therapy. Her social history was noteworthy for the loss of her husband seven years ago. She became somewhat isolated and subsequently planned to relocate out of state to live closer to her children. When specifically asked, she admitted to sleeping poorly, due to nocturia.

Her initial physical examination identified a urinary tract infection, bronchitis, suspected memory disorder, poor balance, and bilateral long-standing hearing loss. Her echocardiogram revealed normal sinus rhythm with evidence of a grade 1 AV block (a common non-life-threatening condition). No atrial fibrillation was noted. Her blood pressure, measured multiple times over several visits, was high (165/80 mm/Hg).

Her Mayo Clinic internist questioned whether she had experienced a small intracranial hemorrhage from one of her falls, causing an increase in her imbalance. She was subsequently referred to neurology for evaluation of falls and stroke risk. She was also seen in neuropsychology, orthopedics, audiology, and otolaryngology.

Her neurologic examination indicated normal strength, coordination, deep tendon reflexes, and sensation. Her Romberg test was negative. Cognitive status was judged appropriate. She did demonstrate anterograde memory loss during her interview (she was unable to recall three words five minutes after being asked to remember them). However, subsequent neuropsychological evaluation indicated age-appropriate cognitive and memory skills, as well as signs of depression.

A magnetic resonance imaging (MRI) scan did not indicate signs of prior stroke, and the mesiotemporal regions appeared normal. There was no evidence for prior cardioembolic events. Rather, a small, enhancing intracanalicular mass was detected in the left internal auditory canal. The mass measured $3 \times 2$ mm and was most consistent with a small vestibular schwannoma (Figure 1).

The otologic examination revealed normal ear canals, tympanic membranes, and cranial nerve function (except for diminished hearing bilaterally). The general head and neck examination was also normal.

The audiogram is shown in Figure 2 and indicated a symmetrical, mild to moderately severe, sloping sensorineural hearing loss. Word recognition was good bilaterally (80% and 88% for the right and left ear, respectively). Tympanometry demonstrated normal type “A” patterns bilaterally. Acoustic reflexes were present within expected limits for the degree of hearing loss, without decay. These results were indicative of cochlear rather than retrocochlear pathology.

The vestibular evaluation consisted of videonystagmography, computerized dynamic posturography (CDP), rotational chair, hyperventilation, positional and vestibular evoked myogenic potentials (VEMPs). Visually guided eye movements (saccade, pursuit, optokinetic, and gaze-holding tests) were normally accomplished, there was no spontaneous nystagmus noted, and caloric responses were strong and symmetric (19% right weakness, 3% directional preponderance). Slow harmonic acceleration tests were within normal limits. There was no evidence
for posterior, horizontal, or anterior canal benign paroxysmal positional vertigo. CDP test results were all within normal limits.

There were only three abnormal test results on the vestibular study. First, there was a 7 degrees/sec right-beating nystagmus in the sitting position with the head turned to the left (measured without visual fixation). Our laboratory limit for horizontal nystagmus in a single head position was 6 degrees/sec; therefore, this was a borderline abnormality. Second, there was an 8 degrees/sec right-beating nystagmus induced by hyperventilation in the caloric position (supine position, head and upper torso elevated 30 degrees). There was no nystagmus in this position before forced hyperventilation was accomplished. Finally, the VEMP absolute latencies for P1 and N1 were significantly prolonged on the left, as shown in Figure 3. These results were interpreted as consistent with a slowly progressive, partially or recently compensated, left vestibular deficit. The delayed VEMP latency was strongly suggestive of a retro-labyrinthine inferior vestibular nerve lesion.

An orthopedic consult was also obtained. Briefly, a healed patella fracture and severe degenerative joint disease were identified in the right knee, causing pain when walking or squatting. The patient was a candidate for total knee replacement.

From the above the following risk factors for falling were discerned:

1. Prior fall history
2. Depression
3. Imbalance from a partially or recently compensated vestibular weakness resulting from a left vestibular schwannoma
4. Right knee pain potentially modifying movement patterns
5. Hypertension treated with antihypertensive medication
6. Urinary tract infection with poor sleep
7. Changed environmental setting (packing belongings to move)

Figure 1. MRI showing the location of a left vestibular schwannoma (large arrow), partially filling the internal auditory canal. The turns of the cochlea, the vestibule (where the saccule and utricle reside), and the posterior semicircular canal (Post.SCC) are labeled. The internal auditory canal (IAC), pons, and fourth ventricle are also labeled.
Taking the above factors into consideration, the recommendation by both the neurologist and the internal medicine consultant was to discontinue the anticoagulation therapy. It was felt that the patient was at high risk for repeated falls, and the potential consequences of a head injury with intracranial bleeding on anticoagulation therapy outweighed the risk of atrial fibrillation–related embolus formation.

**DISCUSSION**

Of the seven risk factors for falling identified, several factors could be modified. However, the overriding risk factor could not. Prior history of falling is the strongest predictor of future falling (Tinetti et al, 1988; Pluijm et al, 2006; Sambrook et al, 2007). Additional risk factors further enhance the risk of falling (Tinetti et al, 1988; Pluijm et al, 2006), but if all of the other risk factors could be modified, her history placed this patient at continued high risk of falling again.

The factor that could be treated acutely would be her urinary tract infection. Though this might not seem to be a strong fall risk, elderly patients often have nonspecific reactions to acute illness, including falling (Schneider and Mader, 2002). With resolution of her urinary tract infection, she will arise less often during the night in the dark to go to the bathroom. Additionally, this may improve her sleeping patterns, indirectly improving alertness and mood.

Factors that might be situational and might therefore improve with time include depression (suspected to be the cause of recent memory and cognitive complaints) and the changing environmental setting.

**Figure 2.** Audiogram showing a bilaterally symmetrical, mild to moderately severe, sloping sensorineural hearing loss with good word recognition and ipsilateral and contralateral acoustic reflexes present within expected limits. There was no evidence for retrocochlear involvement in this study. AC = air conduction; AR-C = acoustic reflex contralateral; AR-I = acoustic reflex ipsilateral; BC = bone conduction; DNT = did not test; MCL = most comfortable listening level; PTA-AC = pure-tone average air conduction; PTA-BC = pure-tone average bone conduction; SRT = speech reception threshold; UCL = uncomfortable listening level.
(moving a household). After her move, she may become more stable simply by improving her mood (improving memory, alertness, and sleep patterns) as well as having an environment that is designed from the beginning to minimize fall hazards.

Factors that will take longer to address include her knee pain and instability from the vestibular deficit. These problems are not likely to go away without some intervention. Long-term vestibular rehabilitation and fall prevention training would likely be beneficial. Knee replacement surgery would minimize pain, at the short-term expense of risking physical deconditioning and vestibular decompensation during the immediate postsurgical recovery period. Additionally, the risk of changes in lower limb sensation would need to be anticipated.

Finally, the hypertension and use of anti-hypertensive medications require close monitoring. Antihypertensive medications increase the risk of orthostatic hypotension, an additional risk factor for falling. However, this risk was offset by decreased risk of cardiovascular and cerebrovascular accident.

Given this fall risk profile, the decision to recommend discontinuing Coumadin therapy seemed warranted. Although the neurologist’s review of the MRI specifically sought and did not find any evidence for prior cardio-embolic events, predicting the multifactorial risks and benefits of anticoagulation therapy was clearly complex in this case. What is more likely—a clot from established heart disease or a cerebrovascular accident from a fall? In this case, the patient did not demonstrate current atrial fibrillation (thought to produce clots) but was clearly falling. The vestibular schwannoma was one factor that tipped the scales in favor of anticipating falls and discontinuing the Coumadin therapy.

From an audiologist’s perspective, this patient’s audiologic evaluation gave no indication of retrocochlear disease. Likewise, her vestibular evaluation revealed modest positional nystagmus, modest hyperventilation-induced nystagmus, and an abnormal VEMP on the involved side. However, the combination of symmetric hearing loss (cochlear nerve, normal) and symmetric caloric responses (horizontal semicircular canal and superior vestibular nerve, normal)

Figure 3. Vestibular evoked myogenic potential (VEMP) waveforms (individual tracings superimposed and superaverages) obtained from right and left ears. The first positive peak, P1, is designated in each superaverage tracing (positivity plotted downward). P1 was delayed by 6.1 msec on the left (ipsilesional) side relative to the normal side. Further, the latency of P1 was beyond the 20 msec cutoff for our laboratory. Peak latency delays seem to be common in patients with retro-labyrinthine involvement. (For specifics on the VEMP recording technique, please see Lundy, Zapala, and Olsheft, in this issue.)
with an abnormal VEMP strongly indicates impairment of the saccule/inferior vestibular nerve. The MRI finding of a left internal auditory canal lesion enhancing with gadolinium was most consistent with a vestibular schwannoma, likely involving the inferior vestibular nerve.

VEMP latency delays seem to be unique to lesions of the eighth nerve, cerebellopontine angle, or lower brain stem (Itoh et al, 2001; Murofushi et al, 2001; Zapala and Brey, 2004). Occasionally, when multiple tests are run, one is likely to be positive just by chance (known in statistics as the problem of the “inflated alpha” when multiple observations are made). With this in mind, in our clinic, we often do not put much weight on solitary VEMP abnormalities if other vestibular tests are not abnormal as well. Delayed-onset latencies for P1 may be an exception to this rule. There are few technical problems that will cause a VEMP latency to be delayed by 4–8 msec relative to the normal side. Longer latency delays (>8 msec) increase the chance that the observed wave is not P1. Given that just fewer than one half of vestibular schwannomas originate in the inferior vestibular nerve, in our clinic, VEMP latency delays are taken as evidence for retro-labyrinthine involvement even in isolation.

In this case, the abnormal VEMP was not an isolated finding. The positional nystagmus that beat away from the involved ear and the hyperventilation-provoked nystagmus were both subtle signs of unilateral vestibular weakness. This is expected when there is a partially compensated unilateral vestibular nerve, in our clinic, VEMP latency delays are taken as evidence for retro-labyrinthine involvement even in isolation.

In this case, the abnormal VEMP was not an isolated finding. The positional nystagmus that beat away from the involved ear and the hyperventilation-provoked nystagmus were both subtle signs of unilateral vestibular weakness. This is expected when there is a partially compensated unilateral vestibular weakness. In cases of incomplete central compensation, positional nystagmus tends to be directed away from the side of the lesion (Leigh and Zee, 1999). Such an asymmetry of vestibular tone can cause vertigo and a tendency to fall toward the side of the lesion (Leigh and Zee, 1999). However, in this case, the co-occurring right knee pain may have also caused the patient to lean toward the left when not paying attention.

Hyperventilation-induced nystagmus may occur in the presence of vestibular schwannoma or demyelinating disease in the posterior fossa (Bance et al, 1998; Walker and Zee, 1999; Carey and Minor, 2001). In the case of a slowly growing vestibular schwannoma, the myelin covering of eighth nerve axons may slowly deteriorate, gradually slowing the nerve’s resting discharge rate (Walker and Zee, 2000; Robichaud et al, 2002). Because the resting discharge rate decreases slowly, the central vestibular system has time to adapt, and common signs of unilateral vestibular hypofunction (nystagmus and vertiginous sensations) do not manifest. However, during forced hyperventilation, axonal conduction can quickly improve as a result of changes in calcium ion concentrations within the cerebral spinal fluid. This, in turn, may result in a sudden, transient increase in the discharge rate of the damaged nerve. Sudden increases in firing rate are interpreted as movement toward the stimulated ear by the central vestibular system. This results in the development of vestibular nystagmus with a fast phase that beats toward the involved ear. In effect, the hypoactive ear appears transiently hyperactive (Walker and Zee, 2000; Robichaud et al, 2002).

Hyperventilation-induced nystagmus with a fast phase that beats away from the involved ear can occur in cases of recently compensated unilateral peripheral vestibular hypofunction (Carey and Minor, 2001). This form of hyperventilation-induced nystagmus is often seen when there is a direction-fixed positional nystagmus observed in other positions. It is thought to reflect simple decompensation of an underlying unilateral peripheral hypofunction, as might be observed with effective tasking. However, in this case, hyperventilation-induced global ischemia (Walker and Zee, 2000) likely provoked the decompensation.

In the present case, the vestibular asymmetry from the vestibular schwannoma was acting as a simple unilateral weakness, and the “demyelination effect” was not observed. However, both depression and anxiety can predispose some people to hyperventilate. When this occurs, or when the cerebral perfusion transiently drops for other reasons (i.e., orthostatic hypotension), the compensated effects of the vestibular schwannoma may become decompensated, resulting in transient dizziness and instability.

It was decided to treat the patient’s vestibular schwannoma conservatively, that is, observation with serial MRI scans without intervention at the present. Vestibular schwannomas are categorized by size (based on imaging) as intracanalicular, cisternal, brain stem compressive, and hydrocephalic. A tumor confined to the
internal auditory canal is defined as intracanalicular, with symptoms limited to hearing loss, tinnitus, and dizziness. As it begins to protrude out of the internal auditory canal and into the cerebellopontine angle cistern, symptoms are still typically audiovestibular, though perhaps to a greater degree. Once it makes physical contact with the brain stem and compresses the pons, trigeminal nerve symptoms (usually diminished corneal reflexes and facial hypesthesias) occur. Ataxia can begin at this stage from brain stem compression. Last, very large tumors can compress the brain stem to such a degree that the fourth ventricle is occluded, impairing cerebrospinal fluid circulation, resulting in hydrocephalus. Symptoms at this stage include all of the above, in addition to visual loss, multiple lower cranial neuropathies, and eventually death from cerebellar tonsil herniation through the foramen magnum.

Current treatment strategies today include stereotactic radiation (gamma knife), surgical removal, or observation with serial MRI scans (or computed tomography scans if MRI is contraindicated). The potential side effects of treatment with stereotactic radiation and surgery include loss of residual hearing, worsening of imbalance, facial nerve palsy, cerebrospinal fluid leak, and trigeminal nerve dysfunction. It is not uncommon for vestibular schwannomas to remain static for years, without any growth. Typically, vestibular schwannomas, when they do progress, grow slowly, with the average being about 1 mm per year. There is certainly variability in growth rate, with relatively few tumors growing rapidly, on the order of 1 cm per year (Nedzelski et al., 1992).

MRI scanning is the modality of choice for assessing the size of vestibular schwannomas. This imaging technique can accurately measure the physical dimensions of the tumor in three planes. Once a vestibular schwannoma is identified by MRI scanning, physiological tests of hearing and balance have a very limited role. These tests correlate poorly with physical tumor size and growth (Jackler and Pfister, 2005).

For this patient, although she had some imbalance attributable to her vestibular schwannoma and secondary vestibular dysfunction, there was agreement among her treating physicians that observation with serial MRI scan was the best course. She is elderly, has other medical morbidities, has no hearing loss characteristic of a vestibular schwannoma, has no central nervous system signs or symptoms attributed to her vestibular schwannoma, has a very small tumor size, and is willing and able to undergo serial MRI scans.

Patients on anticoagulation therapy who are at high risk of falls present a very difficult dilemma. The degree of anticoagulation must be monitored closely by the physician with tests of hemostasis to prevent over- or under-anticoagulation. The underlying reasons for coagulation (dysrhythmia, prior thrombus formation, prior embolic event, physical restriction and inactivity) all have risks for embolic phenomena. Likewise, the causes of imbalance are numerous (prior stroke, cardiac disease, musculoskeletal disease, polypharmacy, vestibular disorder, visual–perceptual disorder, etc.). Hence, the management of patients with anticoagulation therapy and high risk of falls should be individualized. For most patients, vestibular rehabilitation or balance retraining can offer some symptomatic improvement.

This patient was encouraged by her medical team to stay active in order to prevent greater instability resulting from poor central compensation. Vestibular exercises in conjunction with fall prevention and balance retraining were recommended.

In summary, a patient presented with the dual risks of clot formation/cardio-embolic stroke risk and a history of falls, in part due to her left vestibular schwannoma and subsequent deficit. Her Coumadin therapy decreased her embolic stroke risk but increased her risk for fall-induced intracranial hemorrhage. Efforts to identify potentially modifiable fall risks included seven risk factors. Whereas some of these factors could be modified over short and intermediate time frames, some could not. Her overall fall risk profile (and the risk of intracranial hemorrhage while under anticoagulation therapy) was judged to be a higher health risk than the current risk of cardio-embolic stroke. Consequently, it was recommended that she discontinue her Coumadin use.
REFERENCES